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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/527,767	03/17/2000	Wolfgang Kreiss	LeA 33 072	3608

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EXAMINER	
YANG, NELSON C	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 01/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/527,767	KREISS ET AL.	
	Examiner	Art Unit	
	Nelson Yang	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 March 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Claims 27-43 are currently pending.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 27-29, 31-39, 41-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Simpson et al [US 6,117,643] in view of Thastrup et al [US 6,518,021].

Thastrup et al teach the monitoring and recording of quantitative information correlating the spatial distribution or change in the spatial distribution of cell luminescence (column 4, lines 15-30), and further teach that this makes it possible to set up meaningful relationships between the influences of a chemical substance or mixture of chemical substances on cellular systems and the redistribution response in both a fast and reproducible manner (column 3, lines 40-60). Specifically, Thastrup et al teach the detection of intracellular translocation of a component of an intracellular pathway affecting intracellular processes comprising: (a) culturing one or more cells containing a nucleotide sequence coding for a hybrid polypeptide comprising a luminophore linked to the component under conditions permitting expression of the nucleotide sequence, (b) incubating the cell or cells with a substance to be screened for biological function or biological effect, and (c) measuring the light emitted from the luminophore in the incubated cell or cells

and determining the result or variation with respect to the emitted light from said luminophore, such variation being indicative of the translocation of the component in said cell or cells (claim 1). Thastrup et al however fail to teach that the cells are located in a sheet of diffusion controlling matrix selected from the group consisting of secondary valence gels, synthetic polymer gels, and viscous solutions.

Simpson et al, however, teach a biosensor comprising bioreporters enclosed in polymer matrix (column 7, lines 65-67). Simpson et al specifically teach encapsulated cells that can be formed into sheets or thickness or diameter desired, where cells may be added to molten agar or agarose, where gelation occurs as the agar or agarose cools to room temperature (column 68, lines 33-51). Simpson et al further teach that the polymer matrix provides the cells with a greater degree of protection (column 6, lines 45-55), and also teach that encapsulation allows for long term application of the biosensor (column 68, lines 5-20).

Therefore, it would have been obvious to one of ordinary skill in the art for the cells of Thastrup et al to be encapsulated in a polymer matrix, as suggested by Simpson et al, in order to provide the cells with a greater degree of protection and allow for long term application of the biosensor.

4. With respect to claim 28, Thastrup et al teach incubating the cell or cells with a substance to be screened for biological function or biological effect (claim 1). Simpson et al further teach the use of a substrate that contains the matrix (column 3, lines 1-15).

5. With respect to claim 29, Simpson et al teach that the matrix may comprise agar or agarose (column 68, lines 33-51).

6. With respect to claim 30, Thastrup et al teach the use of additional biological sensor materials such as antibodies (column 31, lines 45-48).

7. With respect to claim 32, Thastrup et al teach the use of CHO cells and BHK cells (column 26, example 4).

8. With respect to claim 33, Simpson et al teach the cells may have a second signal transducer to function as an internal control signal, which may serve as a dynamic baseline with which to compare the target signal (column 22, lines 23-32). Thastrup et al also teach the use of multiple probes in cells (column 26, example 4).

9. With respect to claims 34-35, Thastrup et al teach that Hepes buffer was used in the experiments (column 27, lines 10-15. Simpson et al also specify the use of a buffer, and teach the incubation of encapsulated HK44 with groundwater and 0.1xYEPG medium, and the use of simple and complex inducer solutions (column 65, lines 1-28).

10. With respect to claim 36, the use of fluorescent labels is taught by both Simpson et al (column 31, lines 20-35) and Thastrup et al (column 21, lines 50-55).

11. With respect to claim 37, Simpson et al teach that layers of encapsulation can also be produced (column 69, lines 35-40).

12. With respect to claims 38-39, Simpson et al teach that cells may be added to molten agar or agarose of 1% to 5% (column 68, lines 48-50). Therefore, in 50 mL of the agar or agarose, there would be 2 to 10 mL of cells.

13. With respect to claim 40, while Simpson et al teach biosensors comprising bioreporters enclosed in polymer matrix as discussed above, Simpson et al fail to specifically teach that the biosensor has an optical density of 0.6 to 1.4 at 660 nm. However, it has been held that where the

general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 105 USPQ 233.

Therefore it would have been obvious through normal optimization techniques to a person of ordinary skill in the art to obtain a biosensor with an optical density of 0.6 to 1.4 at 660 nm.

14. With respect to claims 41-43, Simpson et al teach that the sheets can be 0.1-2 mm (column 68, lines 39-41).

15. Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over Thastrup et al [US 6,518,021] in view of Simpson et al [US 6,117,643], and further in view of Ribi [US 5,156,810].

The combination of Thastrup et al and Simpson et al teach biosensors comprising bioreporters enclosed in polymer matrix as discussed above. Neither Thastrup et al nor Simpson et al specifically teach polyacrylates as the polymer.

Ribi, however, teaches that polyacrylate is inert and has good electrical insulating properties, is smooth at the molecular level, and has good adhering properties (column 3, lines 27-35).

Therefore it would have been obvious to use polyacrylate as the polymer in the biosensors of Simpson et al, as suggested by Ribi, since polyacrylate is inert and has good electrical insulating properties, is smooth at the molecular level, and has good adhering properties, and therefore would not interfere with the optical detection of the presence of substances.

Response to Arguments

16. Applicant's arguments filed October 17, 2005 have been fully considered but they are not persuasive. With respect to applicant's arguments that adding a microscope detection system would negate the intended utility of the device of Simpson et al, this argument is acknowledged. However, suspending the cells in a matrix would not negate the utility of the device of Thastrup et al, and the advantages of suspending the cells as discussed above would in fact provide motivation for modifying the invention of Thastrup et al. However, since this was not clearly disclosed in the prior office action, the current office action shall not be made final.

With respect to applicant's second argument that Thastrup et al do not teach bring any substance into contact with any spatially discrete area of the sheet of the Simpson reporter material, this is not found persuasive. Specifically, Thastrup et al do teach contacting cells with a substance and determining the spatial distribution or change in the spatial distribution of cell luminescence. Since the cells are part of the sheet of diffusion-controlling matrix, the substance would by default have to come into contact with spatially discrete areas of the sheet.

Conclusion

17. No claims are allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nelson Yang whose telephone number is (571) 272-0826. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571)272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Nelson Yang
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Art Unit 1641

LONG V. LE
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11/22/05